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SPECTROPHOTOMETRIC DETERMINATION OF AMISULPRIDE IN TABLETS BY DIAZOTIZATION COUPLING REACTIONS

Masara NAKTEL[1]

University of Mosul, Iraq

Zeena Z. AL ABDALI [2]

University of Mosul, Iraq

Abstract

A simple and sensitive spectrophotometric methods for assay of amisulpride in pure form and tablets is achieved. Both methods involves the diazotization of amisulpride with nitrite in an acidic medium to produce the corresponding diazonium salt, followed by either coupling with iminodibenzyl (IDB) in acidic medium to give a violet azo dye which showed maximum absorption at 558 nm (method A) or coupling with 7-iodo-8-hydroxyquinoline-5-sulfonic acid (IHQS) in alkaline medium to produce a red azo dye which show maximum absorbance at 522 nm (method B). The two methods have been applied successfully to determine of amisulpride in tablets and also evaluated by applying the standard addition technique.

Keywords: *Amisulpride, Diazotization, Iminodibenzyl, 7-Iodo-8-Hydroxyquinoline-5-Sulfonic Acid, Spectrophotometric Determination*.

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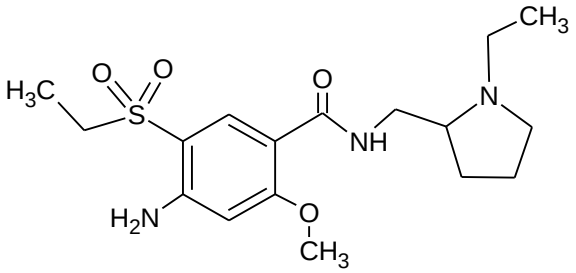
[1] masara.21esp23@student.uomosul.edu.iq, https://orcid.org/0009-0002-0220-9492

[2] zeena.2020@uomosul.edu.iq, https://orcid.org/0000-0002-4526-4574

Introduction

Amisulpride It's a drug has IUPAC name 4-amino-N-[(1-ethylpyrrolidin-2-yl) methyl]-5- ethylsulfonyl-2-methoxybenzamid[1] (Sketch 1), it is a dopamine receptor antagonist belongs to a group of medicines called substituted benzamide antipsychotics used for easing the symptoms in patients of severe or sudden and chronic schizophrenia [2], and treatment of postoperative nauseas and vomiting in adults [3].



Sketch 1: the chemical structure of amisulpride

There are many techniques for the determination of amisulpride including spectrophotometric [4-12], elictrocimical [13-15] and Chromatographic methods [16-20]. The aim from this work is the development of two spectrophotometric methods that are simple, sensitive and accurate to assay of amisulpride in bulk dosage forms and tablet.

Experimental:

Apparatus

The measurements were conducted using Shimadzu UV-Visible 1650 PC Double-beam spectrophotometer with quartz cell (1cm).

Reagent and Solution:

All the chemical compounds were highly pure, and their solutions were prepared as follows:

- Amisulpride solution (100µg/mL): this solution was prepared by dissolving 0.0100 g of amisulpride into100 mL hydrochloric acid (0.1M) in volumetric flask.
- Sodium nitrite solution (1 %): A1.00 g of sodium nitrite was dissolved in 100 mL distilled water.
- Sulfamic acid (3 %):A 3.00 g of sulfamic acid was dissolved in 100 mL distilled water.
- Iminodibenzyl (0.05%):A 0.05 g of iminodibenzyl was dissolved in 100 mL absolute ethanol.
- 7-iodo-8-hydroxyquinoline-5-sulfonic acid (1×10^{-3}M):A 0.107 g of IHQS was dissolved in 100 mL distilled water.
- Hydrochloric acid (1M, 3M): concentrated HCl was appropriately diluted with water to get the required concentrations.
- Sodium carbonate (1M): this solution was prepared by dissolving 10.6 g of sodium carbonate in 100 mL distilled water.

Solution of pharmaceutical tablets *:*

Ten tablets of amisulpride (percepta amisulpride labeled to contain 50 mg amisulpride per tablet) were weighed and powdered. An equivalent amount 0.01 g of amisulpride was taken and extracted with sufficient amount of hydrochloric acid (0.1 M) was transferred to100 mL flask and fill upto the mark with the same solvent and filtered then treated as done in recommended procedure.

Recommended procedure

Aliquots of the working standard solution of amisulpride (0.4 - 14 µg.mL^{-1}) for method A and (0.4-18 µg.mL^{-1}) for method B, were transferred into 25-mL volumetric bottles. In method A, 0.8 mL from 2M hydrochloric acid with 1% $NaNO_2$ (1 mL) were added and the mixture are left for 6 min., then 2 mL of 3% sulfamic acid was added and the solution lives about one min. After that 1mL of 0.05% IDB was added and the volume completed with hydrochloric acid (3M) to the mark. After 5 mint. measure the absorbance versus blank reagent at 558 nm. For the method B, 0.8 mL of 1M hydrochloric acid and 0.3 mL of 1% $NaNO_2$ were added to slandered solutions of amisulpride, the solutions are allowed to stand for 1 min. and 1.2 mL of 3% sufamic acid is added and kept the mixture for one min. then, 1.5 mL from solution (3×10^{-3} M) IHQS was added. The solution was mixed with 3 mL of 1M sodium carbonate solution and diluted to the mark with distilled water. The absorbance measured after 10 min. at 522 nm versus blank reagent.

Result and discussion

Chemistry

Azo dye formation reactions are the most widely applied for the chemical of drug compounds[21] in this methods the drug compound have a primary amino group will diazotization and coupled with reagent contain a powerful electron-donor group, usually phenol or amine. generally, coupling with phenol is achieved in alkaline medium, and with amine in acidic medium [22].

Absorption spectral

Absorption spectrum of the violet azo dye formed with IDB has an absorption maximum at 558 nm and the red azo dye with IHQS has an absorption maximum at of 522 nm while solution blanks have practically low absorption at these wavelengths as shown in Fig.1.

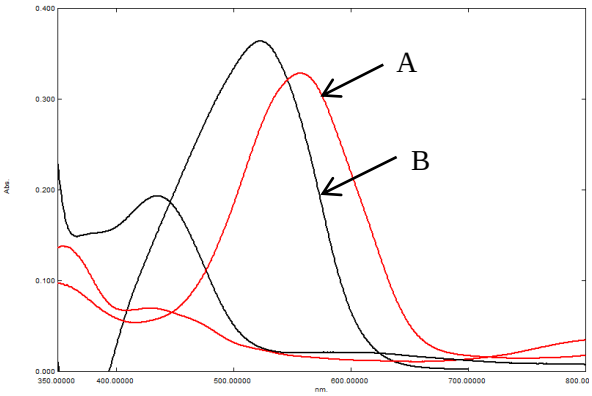


Figure1.Absorption spectra of 6 µg.mL^{-1} of amisulpride, (A) with IDB and (B) with IHQS

Optimization of experimental variables

In order to establish range for quantitative determination of amisulpride in pure forms and tablets, various experimental variables were achieved with 6 $\mu g.mL^{-1}$ at 558 nm and 522 nm in the two methods

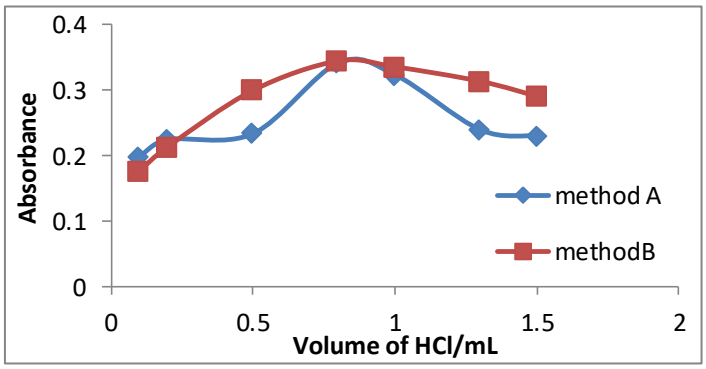
Effect of acid

A variety of acids was use in this experiment. Acids like HCl, HNO_3, CH_3COOH and H_2SO_4, with 1 M concentration were investigated. The results revealed that HCl leads to get the highest absorption for the colored azo dye. The concentration of HCl were studied, the result shown in table 1, indicate that 1 M and 2M HCl leads the greatest absorbance in method A and B respectively.

Table 1: Effect molarity of hydrochloric acid

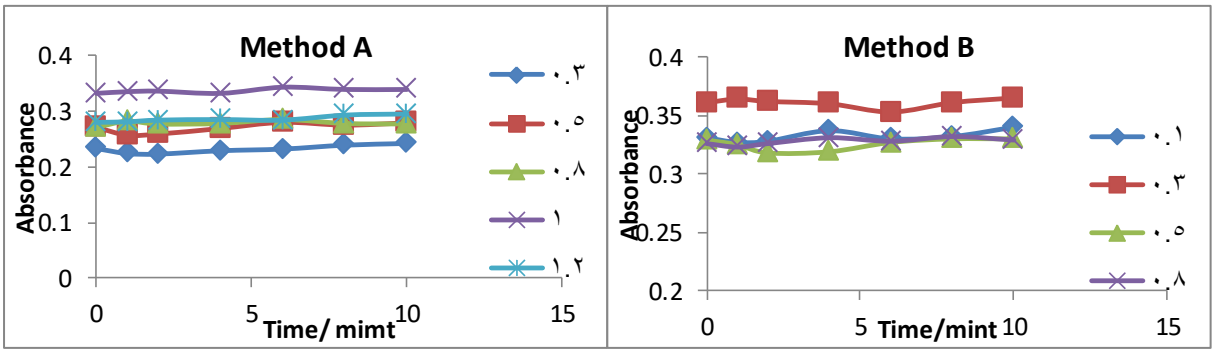
Method	Absorbance / molarity of hydrochloric acid						
	0.5	1	2	3	4	5	6
A	0.233	0.322	0.309	0.285	0.251	0.231	0.197
B	0.254	0.320	0.336	0.300	0.291	0.060	0.026

The effect of various volumes (0.1-1.5 mL) of 1M and 2M HCl on the absorbance of the colored product in method A and B respectively. The results shown in Fig. 2 indicate that 0.8 mL is considered as an optimum volume; therefore, it was recommended for subsequent experiments.



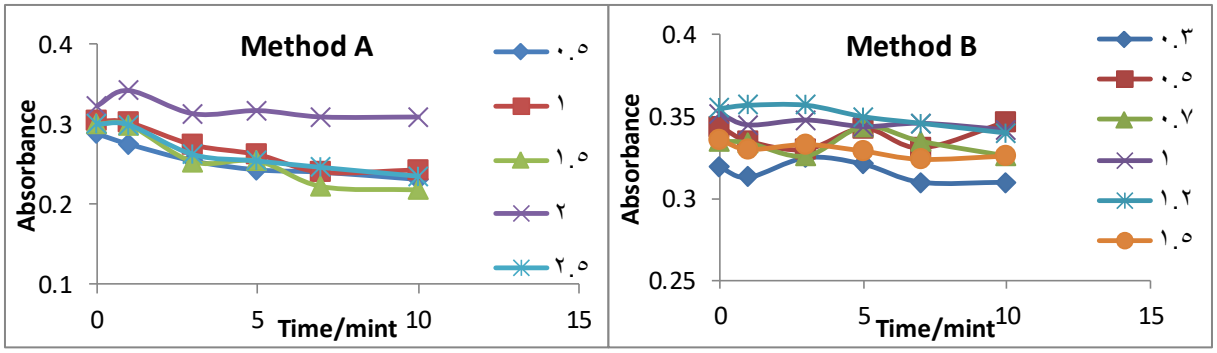
Effect of $NaNO_2$ amount and absorption time

The effect of different amounts of 1% $NaNO_2$with time on the absorbance of colored products has been studied. The results show that 1 mL with 6 min. in method A and 0.3 mL with 1 min in method B are optimums and there are recommended for the subsequent experiments (Fig. 3).



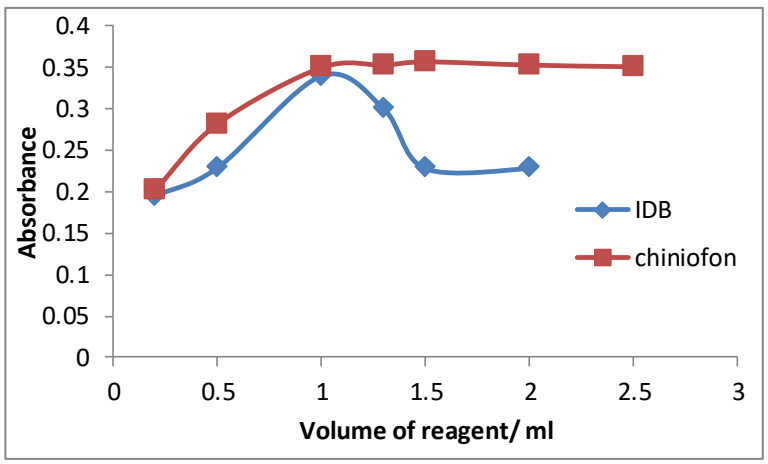
Effect the quantity of sulfamic acid amount and time

The excess of nitrite should be removed by the addition of sulfamic acid. The effect of its amount was studied by using a various amount of 3% sufamic acid solution. The results in Fig. 4 obtained that 2 and 1.2 mL with 1min reaction time in method A and B respectively give the highest absorbance for azo dye and it was fixed in the subsequence experiments.



Effect of reagents

The influence of IDB or IHQS concentration on the color intensity of the product is depicted in Fig 5. the results indicate that the optimum volume of 0.05% of IDB was of 1.0 mL and 1.5 mL of 0.1% IHQS were enough to give maximum absorbance. At a higher concentration from IDB than 2.0 mL , give a turbid solution.



Reaction medium

The development of an azo dyes depends on the nature of reaction medium. In method A the colored azo dye was obtained in acidic medium. The maximum absorbance it was found in HCl medium, this was achieved by using 3M HCl as a diluent as shone in Fig 6(A). Method B the alkaline medium was used for developing intense color. Accordingly a different alkaline solution were tested. Fig. 6 (B) was show that the sodium carbonate suitable alkaline medium for a maximum absorbance.

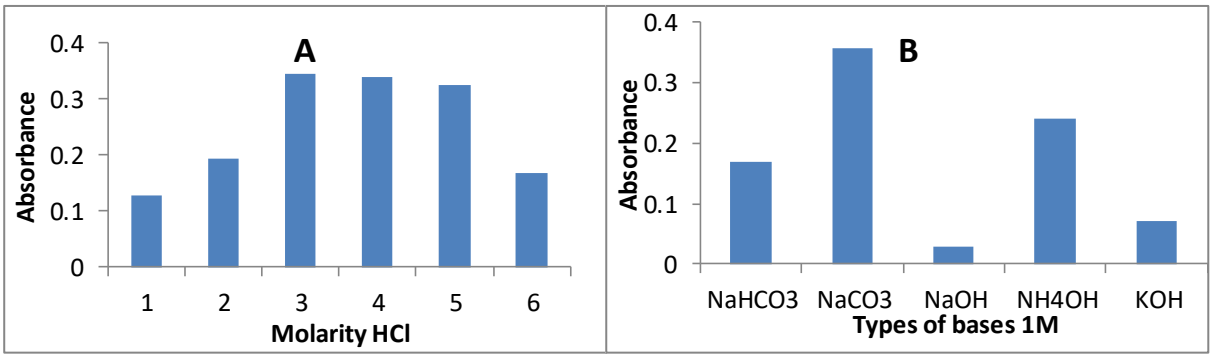
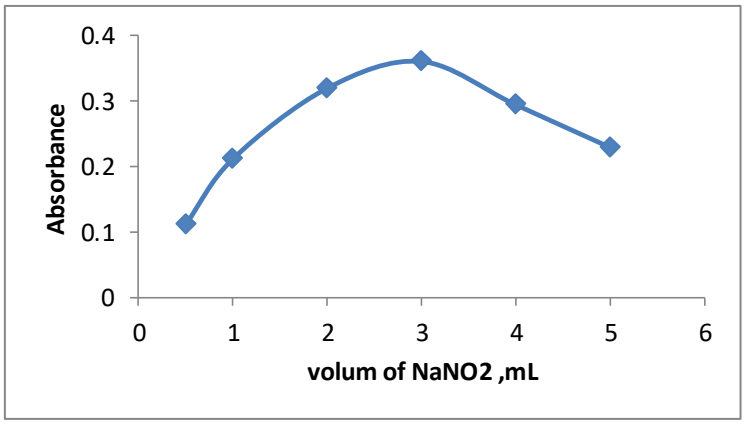


Figure 6. (A) Effect of molarity HCl dilution, (B) effect of type basic solution on the azo dye intense

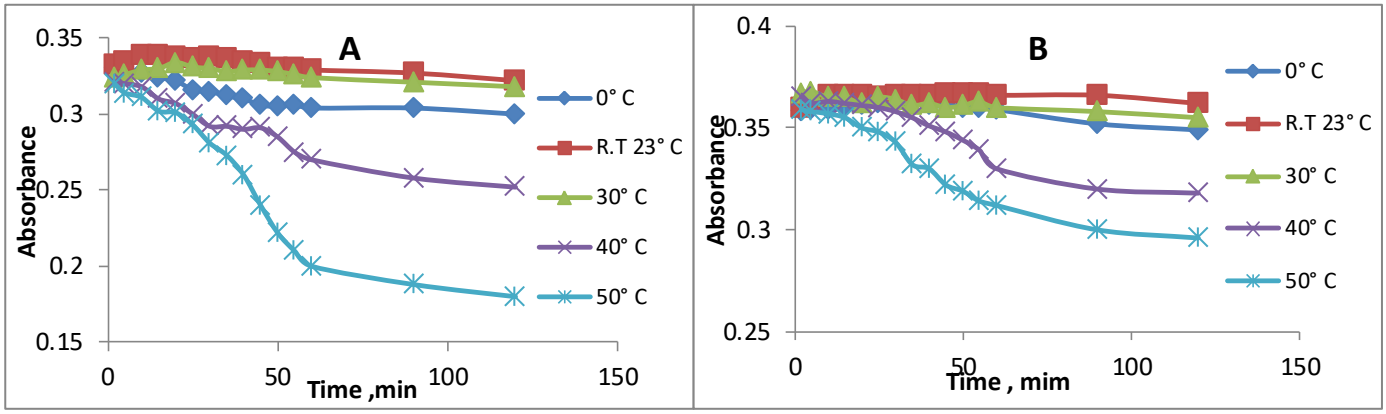
Effect amount of sodium carbonate in method B

The amount effect of (1M) sodium carbonate on the developed colored of product was studied, by taking various volume (0.5-5 mL) of $NaCO_3$, the result in Fig 7 show that 3 m L from base is the best volume.



Effect of temperature and reaction time

According the results in Fig. 8 the intense color dyes was formed as soon as the reagents was added and dilute with 3M hydrochloric acid solution to the mark, in method A or added sodium carbonate solution and dilute to the mark with distilled water, in method B and attained maximum absorption after about 5 and 10 min in method A and B respectively at room temperature (23± 3°C). No cooling was required for the diazotization. The formed azo products remains stable for more than 100 mint.



Calibration graphs

After fixing the optimum conditions for methods A and B, a linear calibration curves is obtained between the absorbance at respective wavelengths and concentration of amisulpride in the ranges are given in Fig.9 and Table 2. The slope, intercept, correlation obtained from different concentrations, quantitation and detection limits of both methods are presented in Table 2.

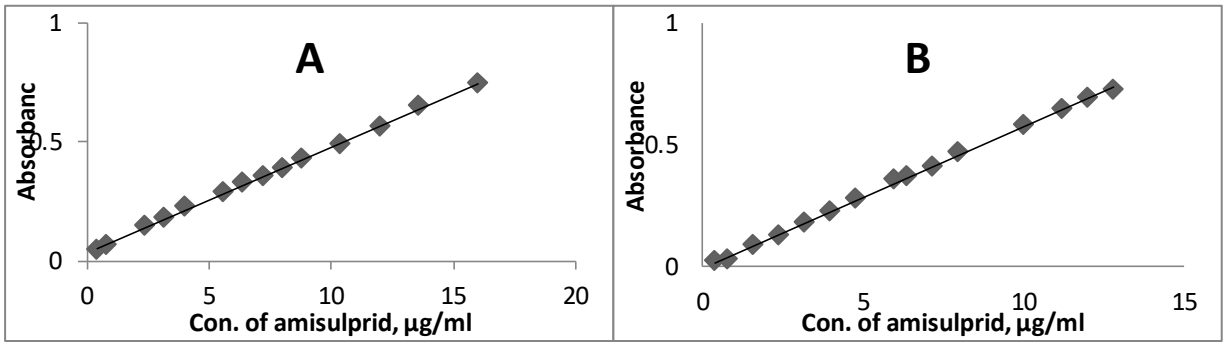


Figure 9. calibration curves for determination of amisulpride with IDB reagent (A) and with IHQS reagent (B)

Table 2. analytical parameter

Parameter	Method A	Method B
ʎ max (nm)	558	522
Linearity range, µ/mL	0.4-16	0.4-12.8
Correlation coefficient R^2	0.999	0.999
Molar absorptivity, L/mol. cm	1.64×10^4	2.13×10^4
Sandels sensitivity, µg/cm^2	0.023	0.017
(LOD)*, µ/mL	0.132	0.130
(LOQ)* µ/mL	0.401	0.394
slope	0.0443	0.0577
Intercept	0.0358	-0.0036

*Average of ten determinations

Precision and accuracy

The precision and accuracy of the two methods were checked through replicate analysis of studied amisulpride at four concentration levels. The results in Table 3. indicate that the recoveries were in the range 99.4-101.2 and RSD were less than 1.3% in all cases, showing good accuracy and repeatability of the proposed methods.

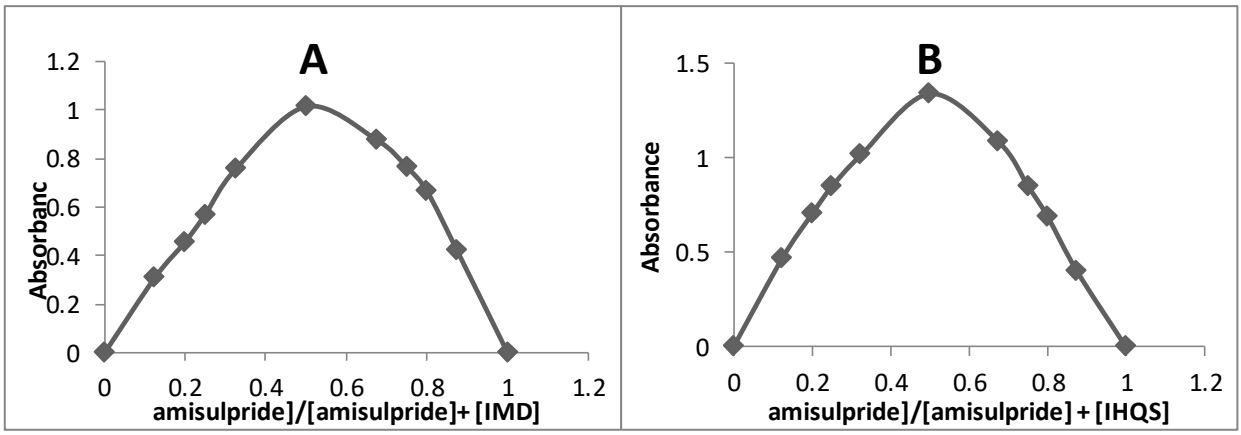
Table3. precision and accuracy of the two methods

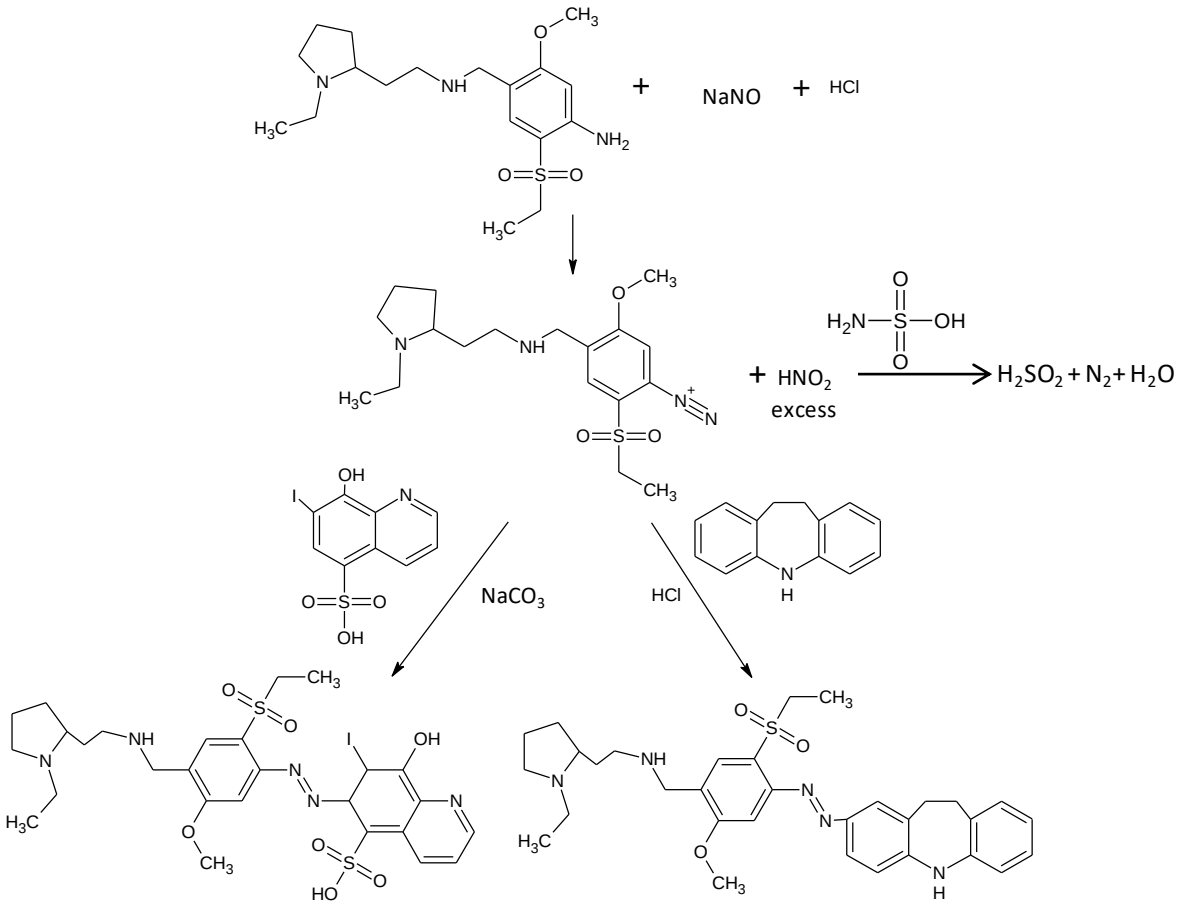
method	Conc. of amisulpride µg/mL	Recovery %*	Relative standard deviation, %*
A	4	99.9	1.217
	6	101.2	0.521
	8	100.1	0.799
	10	100.5	0.597
B	4	100.2	0.729
	6	100.3	0.822
	8	100.2	0.557
	10	99.4	0.470

* Average of five determinations

Stoichiometry of the reactions

The stoichiometry of the reaction between amisulpride and reagents was study by job´s method of the continuous variation [23], the results in Fig.10. showed a 1:1 (diazotized amisulpride: IDB or IHQS). The proposed mechanism of the reactions [24,25] given in scheme 1.





Scheme 2. The suggest mechanism of amisulpride reactions with IDB or IHQS reagents

Application of the tablet dosage form

The proposed methods (A and B) were successfully applied to the estimation of amisulpride in commercially available tablets (percepta amisulpride tablets, MS pharma, Jordan, labeled to contain 50 mg per tablet). The results are compiled in table 4. The good percent recovery value confirms the suitability of the two methods for the routine analysis of amisulpride in tablet.

Table 4. assay of amisulpride in tablet dosage form using the presented methods

	Certified value (mg)	Amount taken (µg/mL)	Drug content found (mg)	Recovery (%)	Average recovery (%)
		1			
Method A	50	2	50.6	101.2	98.4
		4	47.9	95.8	
		6	48.75	97.5	
		8	49.53	98.7	
		10	49.4	98.8	
		1			
Method B	50	2	48.1	96.2	99.4
		4	48.75	97.5	
		6	50.55	101.1	
		8	50.85	101.7	
		10	50.35	100.7	

Comparison of the methods

In order to demonstrate the efficacy the suggested methods and their success in determination of amisupride in tablets, a standard addition technique was used. It has given good recoveries with low relative standard deviation value of amisulpride in tablets (Table 5 and Fig. 10).

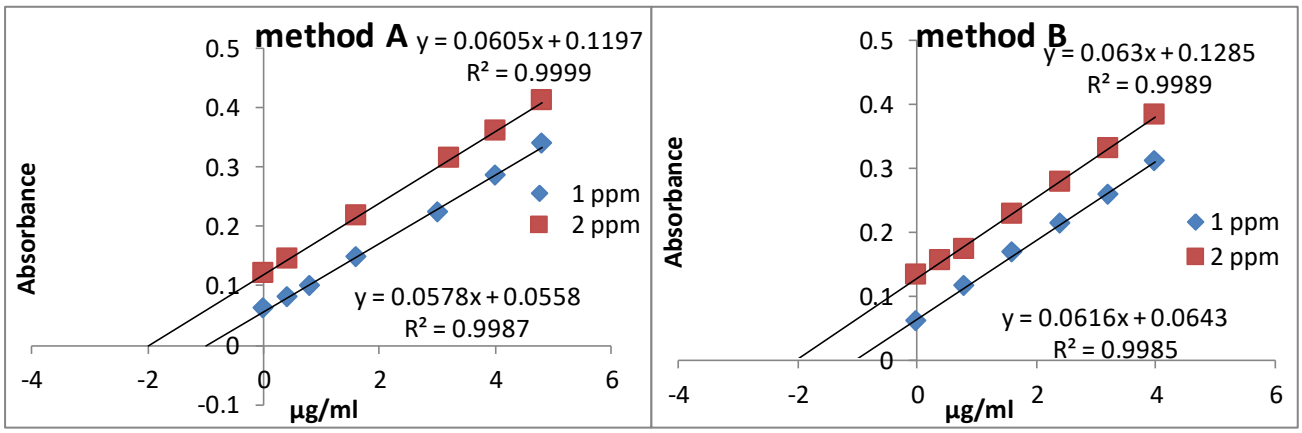


Figure 10: plot of standard addition method to determination of amisulpride in tablet.

Table 5: determination of amisulpride in tablet by standard addition method

Method	Pharmaceutical formulation	Certified value (mg)	Amount present (µg/mL)	Drug content found (mg)	
				Present method	Standard addition procedure
A	percepta amisulpride tablets	50	1	48.27	51.43
			2	50.60	49.46
B		50	1	51.72	52.19
			2	48.10	50.99

Conclusion

This study submitted simple, sensitive and reliable spectrophotometric methods with the advantage of wide ran of determination of amisulpride without heating or organic solvent. These methods have been applied successfully applied to the estimation of amisulpride in pure and tablet.

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